



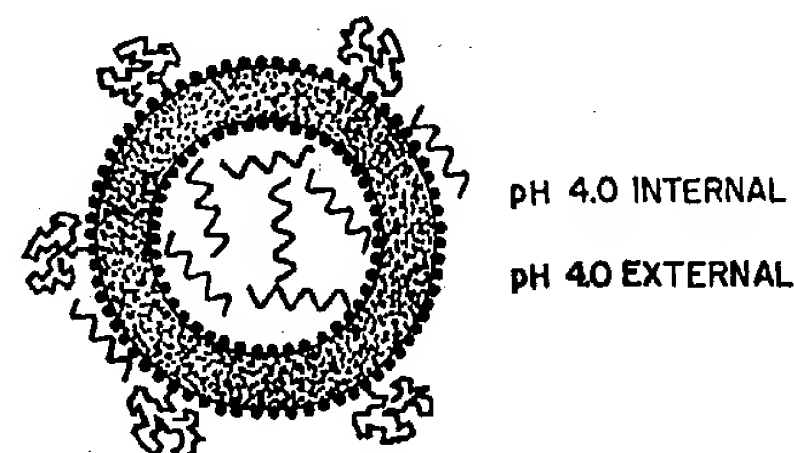
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(54) Title: HIGH EFFICIENCY ENCAPSULATION OF CHARGED THERAPEUTIC AGENTS IN LIPID VESICLES

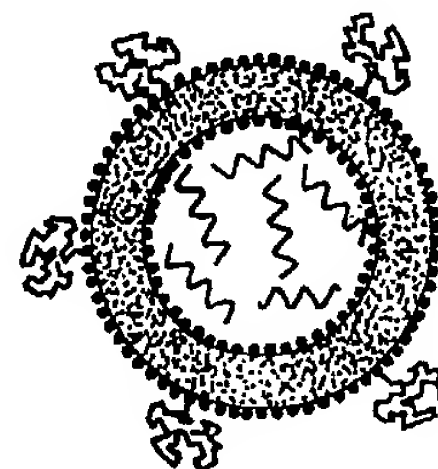
(57) Abstract

Methods for the preparation of a lipid-nucleic acid composition are provided. According to the methods, a mixture of lipids containing a protonatable or deprotonatable lipid, for example an amino lipid and a lipid such as a PEG- or polyamide oligomer-modified lipid is combined with a buffered aqueous solution of a charged therapeutic agent, for example polyanionic nucleic acids, to produce particles in which the therapeutic agent is encapsulated in a lipid vesicle. Surface charges on the lipid particles are at least partially neutralized to provide surface-neutralized lipid-encapsulated compositions of the therapeutic agents. The method permits the preparation of compositions with high ratios of therapeutic agent to lipid and with encapsulation efficiencies in excess of 50 %.



COLUMN CHROMATOGRAPHY

1. EXCHANGE pH 4.0 CITRATE FOR pH 7.5 HBS
2. NEUTRALIZE SURFACE DODAP; ANTISENSE RELEASE
3. REMOVAL OF NON-ENCAPSULATED ANTISENSE

RELEASE OF
SURFACE
ANTISENSEpH 4.0 INTERNAL
pH 7.5 EXTERNAL

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